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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/273,164	03/19/1999	ROBERT MICHAEL ROBERTS		6732

7590

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Steven L. Highlander  
FULBRIGHT & JAWORSKI L.L.P.  
600 Congress Avenue Suit 2400  
Austin, TX 78701

EXAMINER

COOK, LISA V

ART UNIT PAPER NUMBER

1641

27

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/273,164

Applicant(s)

ROBERTS ET AL.

Examiner

Lisa V. Cook

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10-14, 30-35 and 51-183 is/are pending in the application.
- 4a) Of the above claim(s) 51-181 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3-9 and 30-34 is/are rejected.
- 7) ☒ Claim(s) 2, 10 and 11 is/are objected to.
- 8) ☒ Claim(s) 1-8, 10-14, 30-35 and 51-183 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Vacated Finality***

1. Applicant's Supplemental Notice of Appeal filed 1/17/03 is acknowledged. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

## **OBJECTIONS MAINTAINED**

### ***Drawings***

2. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the examiner allows the application. Applicant has deferred corrections until allowance, the objection is therefore maintained.

### ***Information Disclosure Statement***

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant in parent form PTO-1449, cited the references they have not been considered. (For example see pages 71-75). Applicant has not responded to the objection. It is maintained.

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4. The information disclosure statement filed 10/1/99 fails to comply with 37 CFR 1.98(a)(3) because document no. B1 PCT 99/06038 does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. Only the English abstract for PCT 99/06038 has been considered, the full reference has been placed in the application file, but the information referred to therein was not considered. Applicant has not responded to the objection. It is maintained.

## **REJECTIONS MAINTAINED**

### ***Claim Objections***

5. Claims 2 and 10-11 are objected to under 37 CFR 1. 821(d) for failing to recite the SEQ ID NOS. in the claims.

*Please note:* The art rejections below are applied to the claims reading on PAG detection *at about two* months post-partum. The claims reading on PAG non-detection about 60 days post partum.

“about” is warning that exactitude is not claimed but rather a contemplated variation; thus, “between about 25 to 40%” in claim described limits ranging from a chemically operative lower limit to a commercially imposed (for economic reasons) upper limit. *Kolene Corp. v. Motor City Metal Treating, Inc.* (DC Emech) 163 USPQ 214.

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“About” is entitled to latitude in characterizing feature, which was not critical to distinction over prior art. *General Foods Corp. v. Perk Foods Co.* (DC NIII) 157 USPQ 14.

Accordingly Roberts et al. teaching PAG non-detection at 90 days and Zoli et al. teaching PAG non-detection at 80 days read on the instant claims drawn to PAG non detection at about 60 days.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 3, 5, 6, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995).

Roberts et al. evaluate maternal serum concentrations for pregnancy-associated glycoproteins (PAGs) and correlate this measurement to pregnancy in cattle and sheep. (See abstract). The profile of bovine PAG in serum samples from cows revealed that the proteins were expressed just prior to implantation until term (~145 days in sheep, ~280 days in cattle). See page 235.

**II.** Claims 1, 3, 5-6, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Zoli et al. (Biology of Reproduction, 46, 83-92, 1992).

Zoli et al. disclose a double antibody radioimmunoassay for a bovine pregnancy-associated glycoprotein (bPAG). The RIA allowed for PAG measurement in placental extracts, fetal serum, fetal fluids, serum, or plasma samples from pregnant cows. Peripheral serum bPAG levels increased progressively throughout the pregnancy. bPAG levels peaked at days 1-5 prior to parturition and was undetectable at day 100 +/- 20 after parturition.

***Response to Arguments***

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the instant methods ability to detect PAGs unique to early pregnancy) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The cited claims are directed to any and all PAGs, present in early pregnancy and absent about two months post-partum – The prior art teaches such PAGs. Applicant has not distinguished the instantly claimed PAGs from the ones taught in the prior art. The rejections are maintained.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 4, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995) or Zoli et al. (Biology of Reproduction, 46, 83-92, 1992) in view of Sasser et al. (J. Reprod. Fert., Suppl. 37, 1989, 109-113).

Please see discussion of Roberts et al. and Zoli et al. as set forth above.

Roberts et al. and Zoli et al. differ from the instant invention in failing to specifically teach saliva, milk, or urine as samples to evaluate PAG concentrations.

Sasser et al. disclose a radioimmunoassay to detect PAG (also known as PSPB). The samples under investigation-included body fluids other than blood, particularly milk, urine, tears, saliva, vaginal secretions, and cervical secretions. PSPB (Applicants PAG) levels were detected in milk at times when PSPB was excessively high in the plasma of cows.

Although PSPB was not found to specifically react with the antigens used by these investigators in urine, tears, saliva, vaginal secretions, and cervical secretions these mediums were taught as possible samples to evaluate PSPB.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the various known samples (milk, urine, tears, saliva, vaginal secretions, or cervical secretions) taught by Sasser et al. in the method of either Roberts et al. or Zoli et al. to detect pregnancy in a bovine animal, because such samples as taught by Sasser et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing any of the known sample mediums, because these samples were previously considered likely sources for PSPB an indicator of in pregnancy testing for livestock. (page 110, 2<sup>nd</sup> paragraph, Biological Characteristics).

One having ordinary skill in the art would have been motivated to detect PSPB levels in any of these disclosed samples in order to detection bovine pregnancy, because such body fluids were known. Given the diversity of PSPB and its expression (having various possible antigen reactivity), it would have been advantageous to measure different samples for possible PSPB concentrations and relate those measurements to pregnancy.

**II.** Claims 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Aspartic Prot., Struct., Funct., Biol., Biom., Impl., 231-240, 1995) or Zoli et al. (Biology of Reproduction, 46, 83-92, 1992) in view of Xie et al. (Biology of Reproduction 57, 1384-1393, 1997) and in further view of Gerrie et al. (Clinica Chimica Acta, 155, 1986, page 51-60).



The teachings of Roberts et al. or Zoli et al. in view of Xie et al. are set forth above.

Although these references do not specifically state that a double antibody -ELISA procedure is employed to detect PAGs in a bovine sample, it is well known to those with ordinary skill in the art that ELISA assays are commonly used for such a purpose. Methods for determining this data can be achieved by procedures known to those of ordinary skill in the art.

Gerrie et al. teach a sensitive enzyme-linked immunoassay to detect a pregnancy-associated  $\alpha_2$ -glycoprotein. Plates coated with sheep anti-human  $\alpha_2$ -PAG were incubated with the target sample, rabbit anti-human  $\alpha_2$ -PAG, and goat-anti-rabbit IgG peroxidase conjugate. The peroxidase reaction was measured and correlated to PAG concentrations in the sample. (See page 53-54, especially Assay procedure).

It would have been prima facie obvious to one of ordinary skill in the art to determine the amount of pregnancy associated glycoproteins in bovine samples by ELISA as demonstrated by Gerrie et al. in the methods disclosed by Roberts et al. or Zoli et al. in view of Xie et al. with a reasonable expectation of success and little additional labor because this information can be easily determined utilizing reagents (i.e. antibody compositions) that are already being used in their methods.

The ELISA assay procedures employed in the teachings of Gerrie et al. would have been an obvious substitution to the RIA/detection procedures taught by Roberts et al. or Zoli et al. in view of Xie et al. for the detection of pregnancy associated glycoproteins because it is well known to those of ordinary skill in the art at the time of applicant's invention that ELISA produces increased assay sensitivity. This point is seen in the U.S. Patent#4,271,140 – Bunting, which state that double receptors assay improve sensitivity (see abstract and col 2).

This patent is merely cited in support of Examiners position with respect to ELISA protocol sensitivity and assay improvement at the time of applicant's invention. It is not intended to be utilized as part of the instant rejection.

One of ordinary skill in the art would utilize various comparative assay formats for the resulting data sets to evaluated PAG concentrations. These procedures/assay formats are routine optimizations that are almost always determined and used in immunoassay studies. Unless the result obtained in the instant application is a significant and unexpected difference over the prior art, it would have been prima facie obvious for one of ordinary skill in the art to employ known assay protocols in the given parameters to determine the unknown as a means of optimizing the assays provided by the art.

***Response to Arguments***

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the instant methods ability to detect PAGs unique to early pregnancy) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The cited claims are directed to any and all PAGs, present in early pregnancy and absent about two months post-partum – The prior art teaches such PAGs. Applicant has not distinguished the instantly claimed PAGs from the ones taught in the prior art. The rejections are maintained.

### NEW GROUNDS OF REJECTION

*Please note:* The art rejections below are applied to the claims reading on PAG detection *at about two months post-partum*. The claims reading on PAG non-detection at 60 days post partum. However the disclosure does not exemplify any PAGs non-detection measurements at 60 days. Accordingly the rejection under 112, 1<sup>st</sup> paragraph has been applied.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8, 10-14, and 30-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production of pregnancy associated antigens (PAGs), it does not reasonably provide enablement for the claimed method of detecting pregnancy, wherein the PAGs are absent at about two months post-partum. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant has not provided evidence in the specification via examples indicating that the inventive PAGs were measured/absent before pregnancy, measured through-out term, and absent at about two months post-partum.

The specification outlines the structures of the PAGs and renders the relative compositions similar to known PAGs in the prior art, however the actual measurement of the inventive PAG constructs to exhibit their absence at about two months post-partum is not disclosed.

There is no guidance in the specification as to how to determine which PAGs will meet the claimed limitation of being absent at about two months post-partum. The prior art teaches non-detection at 90 days (Roberts et al.) and non-detection at 80 days (Zoli et al.) It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte Forman, 230 USPQ 546 BPAI, 1986.

In absence of guidance and/or working examples, one skilled in the art would reasonably conclude that a PAG (pregnancy associated antigen) could be measure in pregnancy and absent at about two months post-partum. The scope of the claims must bear a reasonable correlation with the scope of enablement. One skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to correlate PAG detection and subsequent non detection at about two months post-partum. It has been set forth above that 1) the experimentation required to determine such PAGs would be great as 2); there are no proper guidance in the instant specification, 4) the nature of the invention is not known in the prior art, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by such non showing, and lastly 7) the claims broadly recite a any PAG with a novel function without specifically stating how this can be done without undue experimentation.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

***Allowable Subject Matter***

9. Claims 182 and 183 with respect to Sequence Identification No.32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
10. For reasons aforementioned, no claims are allowed.
11. New ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE NON-FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Lisa V. Cook

CM1-7B17

(703) 305-0808

3/11/03



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

02/03/03